Jacoby (G. W.)

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EPIBLASTIC ORIGIN

—OF THE—

Central Nervous System.

PRESIDENTIAL ADDRESS DELIVERED AT THE ANNUAL MEETING OF THE NEW YORK NEUROLOGICAL SOCIETY, MAY 1st, 1888, BY

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The Epiblastic Origin of the Central Nervous System.

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BY DR GEORGE W. JACOBY.

[AFTER a few remarks pertinent to his entrance upon the duties of his office, the speaker proceeded as follows.]

When, after impregnation, the remarkable process of segmentation takes place in the germ, the result is the formation of a number of so-called embryonal or indifferent corpuscles, from which the entire protoplasm of the future animal is the direct descendant, but which lack any definite character as regards the formation of future tissue. By the word segmentation is, of course, not meant a breaking up of the protoplasm of the germ into isolated individuals, but it is to be understood that the corpuscles are interconnected during every stage of segmentation, either

by the intervening layers of cement-substance, or by means of delicate off-shoots or bridges. This continuity is a fact which is considered established by almost all modern biologists, whether engaged in the study of animal or in that of vegetable life. The next stage after the completion of segmentation is the division of the germinal spot into layers. This phenomenon has been best studied in the fructified germ of the chick. We know positively that, as a result of fructification, we have the division of the germ into two layers, inclosing a small vacuole or cavity, which two layers are speedily increased by the appearance of a third, between the two original ones. These three layers are of supreme importance in the development of the embryo, and their history is one of the most important points in comparative embryology.

These layers have been termed by Remak*) the ectoderm, close beneath the vitelline membrane, and the entoderm, forming the bottom of the vacuole toward the yolk, whereas to the middle layer filling the vacuole he applied the term mesoderm. Balfour was the first to make any change in this nomenclature, suggesting the terms epiblast for ectoderm, hypoblast for entoderm, and mesoblast for mesoderm, and these terms have been adopted by all English and by a great many German writers on account of their manifest superiority. Ever since the attention of embryological observers has been turned from the mere recognition of changes to the question of their *provenance*, the first stumbling-block has proved to be the origin of the mesoblast.

A large number of investigators maintain that the mesoblast is an offspring of the epiblast; a smaller number, among whom is Balfour†) himself, maintain

*) "Untersuchungen über die Entwicklung der Wirbelthiere," 1850—'55.

†) Foster and Balfour, "Elements of Embryology," London, 1883.

that to the hypoblast alone is due the origin of the mesoblast, and still a third group exists, who, taking the golden path, are willing to allow both the hypoblast as well as the epiblast to participate in this formation. To the view of Peremeschko,*) that the elements of the mesoblast creep or fall through the fenestrated hypoblast from the subjacent white yolk into the space between the original layers, little or no importance can be attached.

A number of modern writers seem to agree that the mesoblast grows from the periphery, *i. e.*, from the germinal wall and the area vasculosa, into the space between these two layers in the primitive streak.

Von Baer,†) and afterward Remak, were the earliest to make an attempt at proving a direct relationship between these layers and the tissues derived from them. Remak proved that the epiblast generated the epithelium of the skin and its appendages, such as the hairs and the sudoriparous and sebaceous glands, the crystalline lens, and the central nervous system; that the hypoblast formed the epithelia of the alimentary canal and its glands; and that the mesoblast gave rise to the vascularized connective tissue and muscles. This theory of exclusiveness was received with great enthusiasm, since no preceding publication had shed so much light upon the functions of the germinal layers and their relation to the parts of the complete organism. But in its turn this special significance has been considerably shaken, A. Kölliker,‡) for instance, comes to the conclusion that it is only the hypoblast that is exclusive in the production of epithelia, whereas the epiblast and the mesoblast are

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*) Peremeschko, "Ueber die Bildung der Keimblätter in Hühnereier," "Wiener Sitzungsbericht," vol. lvii, 1868, p. 499.

†) Von Baer, "Entwicklungsgeschichte der Thiere," "Beobachtungen und Reflexionen," Part i, 1828; Part ii, 1837.

‡) A. Kölliker, "Entwicklungsgeschichte des Menschen und der höheren Thiere," Leipsic, 1876, vol. i.

governed in the formation of tissues only by their location in the germ, and do not possess any inherent qualities in this respect. He says: "In consequence of these considerations, the conviction is irresistibly forced upon us that the significance of the germinal layers is not a histologico-physiological one, but a morphological one. If we start from the premise that originally all embryonal cells as they arise from segmentation are of equal value, then the thesis may be sustained that all three layers, *potentia*, also possess the capability of transformation into all tissues, but, on account of certain morphological conformations, do not manifest this power everywhere." All observers, without exception, admit the fact, shown first by von Baer for the vertebrates and by Kowalewsky for a large number of the invertebrates, that the central nervous system is an offspring of the epiblast, which by all is considered epithelial in nature, and which, beyond a doubt, also produces the epidermis of the skin, its appendages, etc. Only in the batrachians has Stricker seen a separate layer beneath the epiblast, from which he maintains the central nervous system is derived.

The question now forces itself upon us, Can we explain the philosophy of the remarkable fact that the surface layer of the body also furnishes the organs of perception and intelligence ? The answer, it seems to me, must, notwithstanding different views of other writers, be given affirmatively.

The lowest forms of animal life, such as the infusion animalcules, including the amœbæ, lack nerves and nervous system ; nevertheless, they are unquestionably endowed with the capacity of sensation. In an infusion they are always found gathered at that portion which is best supplied with light, and this is the case even in a single drop of fluid. So also will they evade obstacles in their path and react upon the eddy produced in the liquid by an approaching rotifer. Or

let us follow Ferdinand Cohn,*) and scoop into a glass vessel some of the green scum from the surface of the water of a ditch. We shall find in this water innumerable *Euglenæ*, microscopical green, spindle-shaped particles of protoplasm, belonging to the class of *Flagellata*, which have not yet been allotted positively to the animal or to the vegetable kingdom. After a brief period these *Euglenæ* agglomerate at the side of the glass which is turned toward the window. Toward evening they gather upon the surface of the water and crowd together in the shape of green balls. Among the *Euglenæ*, however, are found parasites in the form of spores of *Chrytridium*, which separate from the green balls, and are detected as colorless bubbles. Hereupon a number of offshoots grow out from the periphery of each bubble, and each one is prolonged until it has reached a *Euglena*. The offshoot is then forced into the latter and its interior sucked out. Now I am sure that you will all agree with me if I maintain that these movements of these organisms are due to sensation, be it mechanical or perception of light, and that this sensation is localized in the outermost cover of the animalcule, which cover itself is a layer of living matter, obviously most exposed to the influences of the outer world. It is, therefore, the living matter itself which is endowed with the property of sensation, and which, upon receiving an impulse from without, communicates this impulse to the rest of the organism, whereupon a reflex action, motion, ensues. If now the outermost layer of an animal becomes more resistant by being cornified or calcified, it serves as a protective layer, but at the same time becomes less serviceable for the perception of impressions from without, and when this has occured we easily appreciate the necessity for a more precise localization, which assumes

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*) Professor Ferdinand Cohn, "Lebensfragen," "Wiener med. Press," 1886, p. 1431.

the character of the sense of touch. This sense, according to Lovett,*) was, as early as the fifth century, B. C., declared by Democritus to be the primary sense, and the senses of sight, hearing, and taste were assumed to be differentiations from it.

This localization, then, will take place in the shape of a delicate offshoot, a cilium or flagellum, protruding from the surface of the body, and also penetrating to a certain depth where it is in direct connection with the active living matter — living matter which is certainly more active than that of the surface generally.

Conn and Beyer,†) speaking of the organs of special sense of *Porpita*, describe "ectodermal pockets" filled with "modified ectodermal cells," and they say "from their histological appearance they would seem to be organs of touch. The presence of such long delicate cells, with free ends exposed to the surrounding water, would certainly point to such a function; and their position at the extreme end of the velum would favor the same view. They have no connection with the nerve ganglia above described; not a single nerve cell is to be found in them or in any way connected with them."

These reflections also hold good for the comprehension of localization of sensory impressions, more especially for that of vision.

Here the external layer is depressed in the shape of a pocket or cup, thus producing the earliest known visual organs of low animals, in which this spot is marked, very often at any rate, by an accumulation of coloring matter, and in the majority of these low divisions retains its primitive connection with the epiblast even in the stage of complete development. We furthermore find that the number, as well as the localization in different parts of the body, of such

*) R. W Lovett, "The Development of the Senses," "Popular Science Monthly," 1882, p. 34.

†) H. W. Conn and H. G. Beyer. "The Nervous System of Porpita." Studies from Biological Laboratory, Baltimore

visual organs in low organisms varies considerably. This latter fact certainly goes far to prove the differentiation of these organs from an indifferent basis, and this view is only strengthened by the examination of certain species of worms. In many of the latter species (*Turbelaria*, *Trematoda*, *Nemertina*) we find*) "at that place in which, in those of a higher class, there are well-developed eyes, nothing but pigment spots, symmetrically arranged and situated near the brain." Speaking of the *Annulata*, referring particularly to the *Hirudinea*, Gegenbaur says: "Their organs of vision correspond so remarkably in their construction with those cup-like formations described as organs of touch that a condition seems to be given here in which a specific organ of sense is developed from an indifferent organ of perception formed in the integument."

Obviously a depression of the surface layer is more protected than the surface itself, and may thus remain in a more sensitive or percipient condition than the rest of the surface. These depressions, which lower in the scale were simply pigment spots, in the somewhat higher organisms are found to have a species of lens at the entrance of the pigmented pocket. Strange to say, Gegenbauer is very loath to admit that a pigment spot alone, without any traceable nerve connection, is worthy of being considered as a visual organ, although in other parts of his book, as shown by the citations above given, he virtually acknowledges that such is the case. Similar facts have been established as regards the organ of hearing, which in low forms of animal life is nothing more than a depression of the external layer in the shape of a cup, whose lining is intensified in its perceptibility for waves of sound —that is to say, is supplied with more living matter than the rest of the surface. Here also all special

*) C. Gegenbaur, "Grundriss der vergleichenden Anatomie," Leipsic, 1876, pp. 163—164.

connection between these organs (in low forms of worms) and the central nervous system has been sought for in vain, thus again demontrating the formation of an organ of special sense from an indifferent perception organ.

Here it is not amiss to cite the words of Heitzmann and Bödecker,*) who have expressed these facts as follows: "From an organogenetic point of view we may say that the outer senses of the animal organism, serving for perceptions from the outer world, are formations of the outer investment of the animal, its epiblast. The brain, being the highest perfection of sensual impression, retains its origin from the epiblast. The same may be said of the teeth, which, in some lower order of amphibious organisms, such as *Chelonia*, are nothing but horny ledges, or a thickening of the epithelium. Even at the height of development they retain their genesis from the epiblast, and are, at least as far as the enamel is concerned, derivations from it."

The sensory perceptions, then, being special localizations of sensation and perceptions in general, are the earliest to appear both ontogenetically and phylogenetically, to make use of the terms of Ernst Haeckel.†) Even in the supremely developed organism of man all knowledge of the outer world passes into the body first by means of sensory perception. This is popularly acknowledged, as expressed in the much-cited quotation: "The burnt child dreads the fire." Who has not, in observing the restlessness of the infant, thought that every turn of the head at a noise, every gaze at surrounding objects, the fingering and sucking of all things within its reach, all represented the process of development by means of the senses? To make use of Herbert Spencer's words, "they are

*) Carl Heitzmann and C. F. W. Bödecker, "History and Development of the Teeth," "Independent Practitioner," 1887, p. 455.

†) E. Haeckel, "Generelle Morphologie," 1866.

the first steps in the series which ends in the discovery of unseen planets, the invention of calculating engines, the production of great paintings, or the composition of symphonies and operas." Based upon such personal experience ensues the reasoning, the intelligence. According to this conception, the system serving for sensory perception will be a depression of the outer layer of the body, which in all higher animals is the epiblast made up of epithelia; and, the nervous system being derived from the epiblast, it is implied that the functions of the nervous system were originally taken by the entire skin, and then became gradually concentrated in a special part of the skin, which was finally removed from the surface and became an organ *per se.* In accordance with this, we see in all higher animals the first trace of the future central nervous system as a furrow, along the dorsal aspect of the germ, which is bordered by a slight elevation of the epiblast. The furrow deepens, remaining for a time in continuity with the epiblast, until finally the furrow becomes closed into a tube, having a central caliber and being lined by a single layer of epithelia, severed from the outer epiblast layer of epithelia, and covered with the epithelia of the epiblast, now no longer in connection with the tube. Thus far the development of the central nervous system is identical with the development of the crystalline lens of the eye.

How widely different, however, is the course taken by the epithelia in these two organs! Whereas the epithelia of the crystalline lens become elongated, mainly in the ventral portion of the tube, and remain epithelia throughout life, the epithelia building up the so-called medullary tube, the future spinal cord, rapidly undergo a change in their morphological appearance, beginning with the second day of incubation (chick embryo), and assume the character of medullary or indifferent tissue, Here, therefore, that por-

tion of indifferent tissue which has served for the formation of the epiblast, particularly that part of the epiblast from which the nerve-tube has been produced, has once more retrogressed into the original indifferent form, and has given rise to a tissue which has no title whatever to be termed epithelial—namely, nerve-tissue. A close study of the history of development plainly demonstrates that such oscillations, such a rise and fall, are very frequent in the formation, more especially in the transformation, of tissues. Such fluctuations are best observed in the development of bone-tissue. The medullary tissue produces cartilage in the notochord, from which we know the bodies of the vertebræ are subquently produced; but cartilage never produces bone-tissue directly; it first returns to its medullary or indifferent condition, and then, and only then, produces bone-tissue. These same oscillations are common occurrences in the growth of any tissue where the increase in bulk does not take place directly, but by the intermediary stage of medullary corpuscles. I therefore again reiterate that nerve-tissue has no title whatever to the appellation "epithelial" except in the very earliest stages of its formation. This reiteration is all the more necessary because it has been attempted to carry the theory of the exclusiveness of the three germinal layers so far as to call even nerve-tissue, because it is formed from the epiblast, epithelial in nature. No less an authority than Balfour* himself has made such a capricious statement. He maintains that the so-called ganglion cells have been evolved from simple epithelial cells of the epidermis, and that their offshoots, the axis-cylinders, may be considered as offshoots of epithelia.

He also speaks of "epithelial cells" in the act of becoming "nerve cells," and, furthermore, maintains that the spinal nerves are outgrowths from the cen-

*) Balfour, F. M., "An Address," "Nature," London, September, 1880, p. 417.

tral nervous system, and grow thence through the mesoblast to the periphery of the body. These views are all the more surprising since Balfour, as already stated, allows that the mesoblast originates from the hypoblast, thus admitting that connective tissue and muscle may arise from purely epithelial tissue; but because the nervous system arises from the epiblast he says that this nervous system must be epithelial, which, to be logical, he ought also to allege for connective tissue and muscle.

Mihalkovics,† in a few specimens, saw some epithelial-like formations lying at the bottom of the furrow formed in the epiblast, and from this he assumes the formation of the epithelia of the central canal. Such formations were absent in all the specimens that I have studied, and certainly at the fifth day of the chick embryo there is no trace of a lining epithelium around the central canal. In fact, all these views become untenable in view of the facts which the study of embryology reveals.

On the fifth day after incubation (chick) we unmistakably see the tissue which is sharply defined as the future spinal cord to be composed of a mass of protoplasm, with faint indications of agglomerations into medullary corpuscles; even the nerves, more especially the vagus, which is the earliest discernible, is not a nerve proper, but a tract of medullary corpuscles. Only very much later do ganglionic elements appear at all. We know, for instance, that in the human embryo no motor ganglia are present in the spinal cord prior to the third month of embryonal life, and that even in the new-born the number of ganglionic elements in the gray substance is very small, so that the great majority are obviously formed after birth. It is, therefore, astonishing that the fact has been overlooked that between the original epithe-

†) Mihalkovics, V. von, "Entwickelungsgeschichte des Gehirns," Leipsic, 1877, p. 12.

lia and the late ganglionic corpuscles there has existed a retrograde stage of absolute indifference. We can not compare ganglionic corpuscles with epithelia, knowing, as we do, that each ganglionic element is made up of a certain number of medullary corpuscles. We know, also, from the history of development, that the gray substance of the central nervous system appears first in the form of indifferent protoplasm, in which thread-like tracts make their appearance, the future axis-cylinders, long before any medullated nerve is visible. Can we consider the white substance an epithelial one, since we know that it is freely mixed with connective tissue, the neuroglia, and blood-vessels? How is it possible to understand the presence of so great a number of blood-vessels, which are of mesoblastic origin, throughout the gray substance, if the latter is epithelial in nature? The theory presupposing an immigration of mesoblastic elements into the gray substance is an entirely gratuitous one, since we observe in other parts than the nervous system the new formation of blood-vessels independently of other blood-vessels and in no connection whatever with blood and its vessels. Bearing upon these questions are the interesting observations of Heitzmann and Bödecker,* showing the formation of nerves in peripheral portions of the body (in the pulps of teeth) entirely independently of all previously formed central nerves.

I can see no escape from this dilemma unless we assume that that portion of the epiblast which serves for the production of the nervous system has entirely lost its epithelial nature and has returned into the stage of indifference in which it is impossible to decide whether a tissue is epithelial, therefore epiblastic, or connective tissue, that is, mesoblastic. Morphologically, I look upon the gray matter of the central

*) Carl Heitzmann and C. F. W. Bödecker, "Contributions to the History of the Development of the Teeth," "Independent Practitioner," p. 1. 1888.

nervous system as such an indifferent substance—namely, pure protoplasm—and I am convinced that all endeavors of histologists to establish a differentiation between purely connective tissue and purely nervous tissue in this gray matter are useless and will remain ineffectual.

The phylogenetic order of development of the sensory organs of the higher animals is not identical with that of the lower ones. In the latter the depression of the epiblast which serves for a special sensory function is the primary, whereas in the former the depression of the epiblast for the central nervous system is first formed, while the retina, the labyrinth, etc., are secondary formations. Nevertheless, the epiblast participates primarily in the formation of the lens and of the auditory canal.

The cerebrum, being the seat of association and intelligence, is entirely a secondary formation, arriving at its full development in direct dependence of the knowledge gained through sensual impressions, this being the case not only in the higher classes of animals, but also in single individuals. In my conviction, the history of the development of the central nervous system is intelligible only upon the following grounds: (1) That its earliest stage is a depression of the epiblast, in concordance with depressions of the surface layer of lower organisms, for sensory perceptions; (2) that the central nervous system, being an offspring of the epiblast, is epithelial in its origin and so remains *only for the earliest periods of embryological development;* and (3) that the original epithelium returns to a stage of morphological indifference in which it remains during life, composing the gray substance of the central nervous system.